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(54) **Plastics Medicament Containers**

(57) A container 1 made of low-density polyethylene coated on at least one side with a sealant film has an outlet 4 which is closed by a closure tab 5 which can be permanently separated from the remainder of the container along a weakened portion 6 for dispensing one dose of a medicament such as 0.5 to 5g of an anti-inflammatory steroid formulation contained therein. A plurality of such containers can be connected at the tab and/or body to form a strip. The film, which may be derived from cellulose, an acrylic resin, or polyvinyl chloride, is formed by coating with a solution, dispersion or foam of the polymer in a suitable medium after pre-treating the substrate polyethylene by corona discharge, ionising radiation, or an oxidising agent. The coating operation is preferably performed after filling and closing the containers.

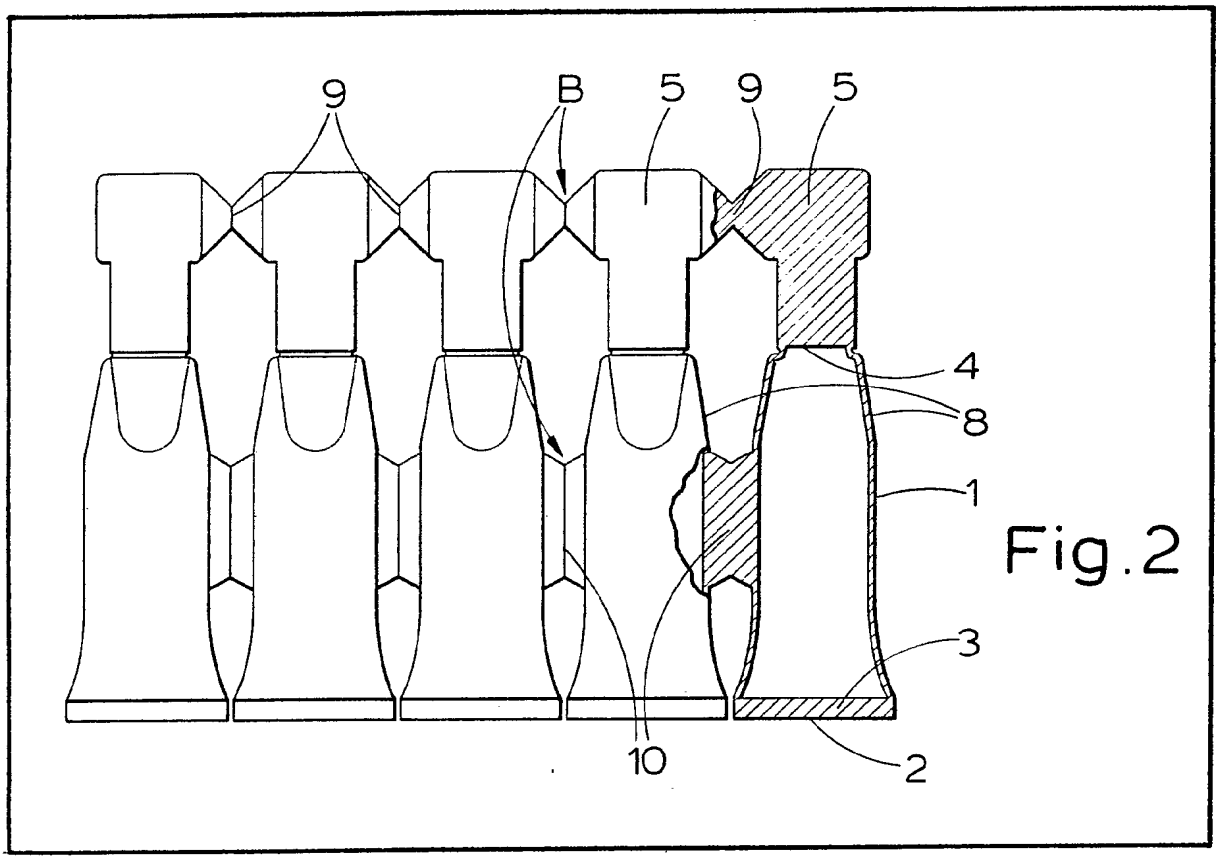

Fig.2

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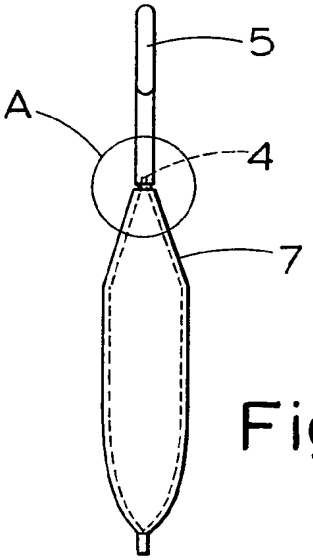

Fig.1

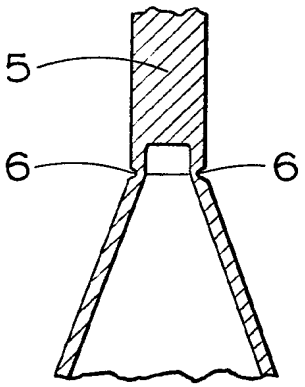

Fig.3

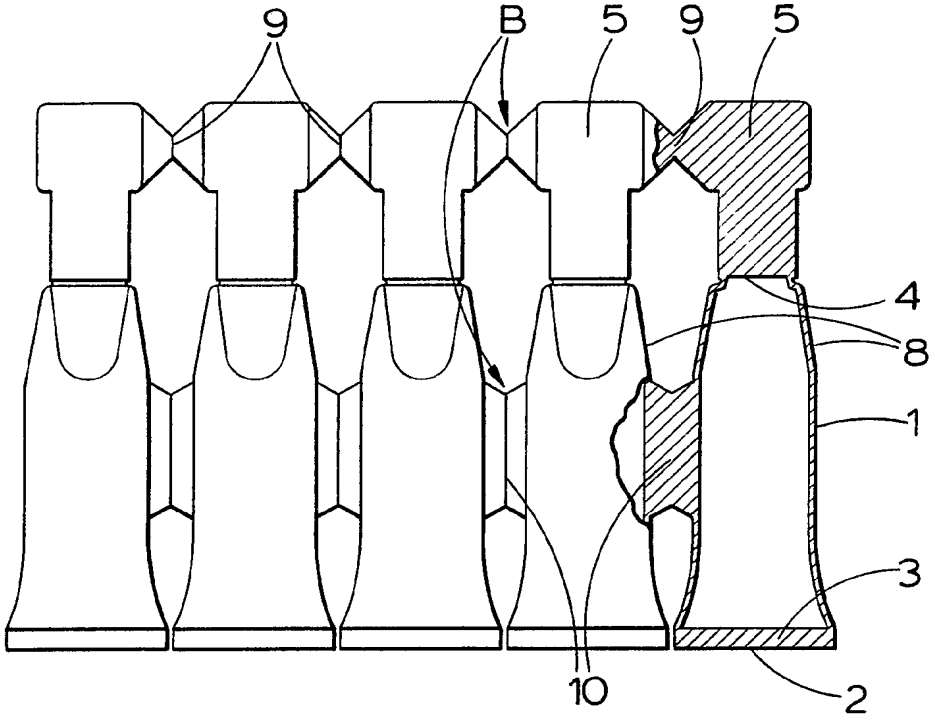

Fig.2

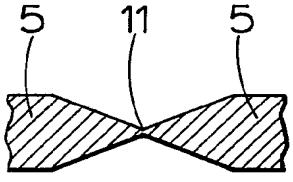

Fig.4

SPECIFICATION
Container

This invention relates to a dispenser or container for the topical application of a medicament, for example an anti-inflammatory steroid.

One of the problems in the topical application of a medicament in semi-solid dosage form (for example creams and ointments) is to try to ensure that the correct dosage is applied. Furthermore, in the case of some medicaments, such as anti-inflammatory steroids, over application may produce undesirable side effects. An object of the present invention is to assist in ensuring that the correct dosage is applied.

According to one aspect of the invention there is provided a container of a flexible plastic material, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein a medicament in semi-solid dosage form suitable for topical application, the amount of medicament present being such as to be suitable for a single application.

According to another aspect of the invention there is provided a container of a flexible plastic material, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein a medicament in semi-solid dosage form suitable for topical application, the amount of medicament being from 0.5 to 5.0 g.

The tab is preferably of such a size that it may be easily gripped between a thumb and a finger of a user to enable it to be readily separated from the container body. In a preferred embodiment at least two opposite sides or edges of the container taper internally towards the outlet. The outlet may be any convenient shape such as elongate, circular or elliptical, but is more preferably an elongate slit.

A preferred material for the container is a tearable plastic material, for example, low density polyethylene. Where the material used for the container is permeable to the medicament or a component thereof, the container is coated on at least one side with a sealant film.

In one aspect of a preferred form, the invention provides a container of flexible low density polyethylene coated on at least one side with a sealant film, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein an anti-inflammatory steroid formulation in ointment form suitable for topical application, the amount of formulation present being in a quantity such as to be suitable for a single application.

In another aspect of a preferred form, the invention provides a container of flexible low density polyethylene coated on at least one side with a sealant film, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein a steroid formulation in ointment form suitable for topical application, the amount of formulation present being from 0.5 to 5 g.

The invention also provides a "strip" of a plurality of containers according to the invention joined together at the tab end and/or body of the container in a way which permits a container to be readily separated from an adjacent container in the strip.

The invention is illustrated in the accompanying schematic drawings in which:

Figure 1 is a side elevation of a unit dose container,

Figure 2 is a sectional view of a plurality of containers joined to form a strip thereof,

Figure 3 is an enlarged detail view of the part ringed at "A" in Figure 1, and

Figure 4 is a detailed sectional plan view of the portion indicated at "B" in Figure 2.

The unit dose container illustrated in the drawings is made of low density polyethylene, for example Alkathene 19 ("Alkathene" is a Trade Mark). With certain formulations, however, one or more of the components present may permeate completely through the polyethylene, and so as to avoid contamination of the external surface the outside is coated with a suitable film coating.

For example, ointments for the topical application of anti-inflammatory steroids contain oily materials e.g. paraffins such as liquid paraffin and/or white soft paraffin or yellow soft paraffin, and we have found that the low molecular weight products or fractions thereof permeate the polyethylene. Therefore, the film that is applied to the container must be non-permeable to these products and capable to adhering to the polyethylene surface.

Suitable film coatings include hydrophilic films such as those derived from cellulose, e.g. hydroxy propylmethylcellulose. Other suitable materials include acrylic resins such as copolymer of methacrylic acid and methylacrylic acid methyl ester, or dimethylaminoethyl methacrylate and a neutral ester of methacrylic acid, co-polymers of vinylidine chloride with vinyl chloride, acrylonitrile, acrylates or methacrylates, or polyvinyl chloride.

The films are formed by coating the container with a solution or dispersion of the polymer in a suitable medium. For example, the hydrophilic films may be applied using an aqueous medium or organic solvents such as an alkanol, e.g. isopropanol and/or a haloalkane e.g. methylene chloride.

In addition the coating material may also contain a plasticizer such as a polyethyleneglycol,

glyceryl triacetate, a polypropylene glycol, sorbitol, dibutyl phthalate or castor oil. The following are examples of specific coating formulations:

Example 1

	% w/w
Hydroxy propyl methyl cellulose	6.0
Polyethylene glycol 6000	0.6
Freshly distilled water to	100.0

Example 2

Hydroxy propyl methyl cellulose	1.75
Propylene glycol	0.2
Isopropyl alcohol	30.0
Methylene chloride to	100.0

Example 3

Eudragit L30D (an aqueous dispersion of an anionic polymer synthesised from methacrylic acid and methylacrylic acid methyl ester)	97.0 or 92.5
Glyceryl triacetate	3.0 or 7.5

Example 4

Eudragit L30D	97.0 to 94.0
Polyethylene glycol 6000	3.0 or 6.0

Example 5

Eudragit L30D	50.0
Eudragit E30D (an aqueous dispersion of a cationic copolymer synthesised from dimethylaminoethyl methacrylate and other neutral methacrylic acid esters)	50.0

Example 6

Eudragit E30D	100.0

Example 7

Eudragit L (as for L30D but the resin is dissolved in organic solvents)	47.5
Glyceryl triacetate	3.0
Polyethylene glycol 6000	1.0
Water	2.0
Isopropyl alcohol	to 100.0

In order to coat the container the surface of the plastic must first be subjected to a preliminary treatment. This may be achieved by a variety of methods, for example, by flaming corona discharge, ionising radiation or treatment with an oxidising agent. A solution, dispersion or foam of the film coat material is then applied to the surface and dried. The coating may be applied by a variety of methods, for example, dipping or spraying. If desired, more than one coat may be applied. Preferably the coating operation is carried out after the container has been filled and closed.

The container comprises a body 1 which is open at one end, herein considered the bottom end 2, during manufacture but is closed after filling by pinching together opposite walls of the container as indicated at 3 (Figure 2). The body of the container has an elongate outlet slit 4 which is normally closed by a tab 5. Where the tab is joined to the body of the container, there is a weakened portion 6 (Figure 3) so that it can be readily separated from the remainer of the container. For this reason, the tab 5 is of such a size that it can be gripped between the finger and thumb of a person using the container. The container tapers towards the elongate slit as shown at 7 and 8 in Figures 1 and 2. After the tab has been removed it may, if desired, be used to spread the medicament on the part of the patient being treated thereby.

The container preferably forms part of a "strip" or plurality of identical containers joined together at the tab at 9 and at the body at 10. The plastics material at the place of join is of reduced thickness as shown at 11 (Figure 4) to enable two adjacent containers to be separated from each other.

Suitable anti-inflammatory steroids for use in such a container include:
beclomethasone 17, 21 dipropionate
betamethasone 17, 21 dipropionate
fluocinolone acetonide
fluocinonide
fluprednylidene acetate
desonide

fluclorolone acetonide
diflucortolone 21-valerate
flumethasone 21-pivalate
flurandrenolone
halcinonide
triamcinolone acetonide
flucortolone 21 pivalate and 21 hexanoate
hydrocortisone 17 butyrate
amcinonide
trimexolone
particular useful anti-inflammatory steroids for use in such a container are:
betamethasone 17 valerate
clobetasol 17 propionate
clobetasone 17 butyrate
hydrocortisone.

The amount of anti-inflammatory steroid in the pharmaceutical formulation in the container is preferably between 0.005—1% more preferably 0.01—0.25%.

In addition to the anti-inflammatory steroid, the formulation may contain at least one other active ingredient such as a local anaesthetic, antibiotic, anti-bacterial, anti-microbial or anti-fungal agent, such as gentamycin, nystatin or neomycin.

Although the foregoing description has concentrated on the use of the container for steroid formulations, it can be used also for other medicaments, for example, anti-bacterial, anti-microbial and anti-fungal formulations. The container can also be used for skin care products, for example, those used for treating nappy rash and bed sores, and in the context of the present invention the term "medicament" is to be understood as including skin-care products.

The active ingredient or ingredients may be formulated in a conventional manner, for example to form an ointment or cream.

Preferably the containers are of such a size that they contain between 0.5 and 5.0 g of the formulation, more preferably 0.5 to 2.0 g. The amount contained may be appropriate for a single dose, but it may be the case that at least some patients will require a plurality of containers to provide a single application or only part of the contents of a container, for example, half of it, to provide a single application.

Claims

1. A container of flexible plastic material, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein a medicament in semi-solid dosage form suitable for topical application, the amount of medicament present being such as to be suitable for a single application.

2. A container of flexible plastic material, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein a medicament in semi-solid dosage form suitable for topical application, the amount of medicament being from 0.5 to 5.0 g.

3. A container according to claims 1 or 2, wherein the closure tab is of such a size as to be grippable between a thumb and a finger of a user to enable it to be separated from the remainder of the container.

4. A container according to any preceding claim, wherein the container has at least two opposite sides or edges which taper internally towards the outlet.

5. A container according to any preceding claim, wherein the said outlet is an elongate slit.

6. A container according to any preceding claim, wherein the said plastic material is permeable to the said medicament or a component thereof and is coated with a sealant material on at least one surface thereof.

7. A container according to claim 6, wherein the sealant material is hydroxy propyl methyl cellulose.

8. A container according to any preceding claim, wherein the said plastic material is tearable.

9. A container according to claim 8, wherein the said plastic material is low density polyethylene.

10. A container according to any one of claims 1 to 8, wherein the said medicament contains an anti-inflammatory steroid.

11. A container according to claim 10, wherein the steroid is selected from betamethasone 17 valerate and clobetasol 17 propionate.

12. A container according to claim 10, wherein the steroid is selected from clobetasone 17 butyrate and hydrocortisone.

13. A container of flexible low density polyethylene coated on at least one side with a sealant film, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein an anti-

inflammatory steroid formulation in ointment form suitable for topical application, the amount of formulation present being in a quantity such as to be suitable for a single application.

14. A container of flexible low density polyethylene coated on at least one side with a sealant film, the container having an outlet which is closed by a closure tab which can be separated from the remainder of the container permanently providing an outlet, the container having therein an anti-inflammatory steroid formulation in ointment form suitable for topical application, the amount of formulation present being from 0.5 to 5.0 g.

15. A container substantially as herein described with reference to the accompanying drawings.

16. A plurality of containers as claimed in any preceding claim joined together to form a strip of containers in a way which permits a container to be separated from an adjacent container in the strip.

17. A plurality of container, as claimed in claim 16, wherein the container are joined together at their tabs.

18. A plurality of containers, as claimed in claim 16 or 17, wherein the containers are joined together at body portions thereof.

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